Omega Therapeutics Announces Publication of Epigenomic Controller OTX-2002 Preclinical Data in Nature Communications

September 17, 2024 11:00 AM EDT

- *Treatment with OTX-2002 led to controlled downregulation of MYC gene expression and resulted in significant inhibition of tumor growth as a monotherapy and in combination with standard of care agents in preclinical models of HCC*
- *Proof-of-concept data for OTX-2002 support potential of epigenomic controllers to effectively target and modulate expression of nearly any human gene, including historically undruggable targets*
- *Data further validate the OMEGA platform's potential to rapidly and prospectively design, develop and advance programmable epigenomic mRNA medicines for the treatment of a broad range of diseases*

CAMBRIDGE, Mass., Sept. 17, 2024 (GLOBE NEWSWIRE) -- Omega Therapeutics, Inc. (Nasdaq: OMGA) ("Omega"), a clinical-stage biotechnology company pioneering the development of a new class of programmable epigenomic mRNA medicines, today announced the publication of preclinical data from studies of OTX-2002 in *Nature Communications.* The article highlights the potential of Omega's approach to precision epigenomic control and the ability of OTX-2002 to controllably regulate the historically undruggable MYC gene in multiple models of hepatocellular carcinoma (HCC), the most common type of primary liver cancer.

"These proof-of-concept data demonstrate that by combining cutting edge understanding of DNA architecture and epigenomic regulation with our OMEGA platform, we can rapidly and prospectively design an epigenomic controller to lay intended epigenetic marks to controllably target nearly any gene and tune its expression," said Mahesh Karande, President and Chief Executive Officer of Omega Therapeutics. "These preclinical data show OTX-2002's exquisitely specific engagement of c-MYC, a master oncogene that has proven challenging to regulate by other modalities, resulting in its downregulation at the mRNA and protein level and robust anti-tumor effects across multiple preclinical HCC models. We believe this publication, along with the promising preliminary clinical data generated from our ongoing MYCHELANGELO™ I trial, further validates the capabilities of the OMEGA platform to develop programmable epigenomic mRNA therapeutics to potentially address a broad spectrum of diseases."

OTX-2002 is a first-in-class, bicistronic mRNA-encoded epigenomic controller (EC) delivered via liver-targeting lipid nanoparticles that is designed to durably downregulate MYC expression pre-transcriptionally via two different epigenetic modifications at two distinct genomic loci within the MYC gene. MYC is a master transcription factor that regulates cell proliferation, differentiation and apoptosis and plays a significant role in more than 50% of all human cancers.

Key Findings

The publication, titled "*Targeted Transcriptional Downregulation of MYC Using Epigenomic Controllers Demonstrates Antitumor Activity in Hepatocellular Carcinoma Models*," describes OTX-2002 and its effects on tumor growth in cellular and animal models of HCC. Treatment with OTX-2002 resulted in the following:

- Rapid reduction in both MYC mRNA and protein levels
- Decreased viability of multiple HCC cell lines
- Dose-dependent reduction in tumor size and growth rate in preclinical models of HCC
- Antitumor activity and mechanism of action that is synergistic when combined with either tyrosine kinase inhibitors or immune checkpoint inhibitor agents
- Beneficial impact on the tumor microenvironment in immune-competent mice bearing HCC tumors as evidenced by a decrease in inhibitory regulatory T cells

OTX-2002 is currently under clinical evaluation in the Phase 1/2 MYCHELANGELO™ I trial in adult patients with HCC and other MYC-associated solid tumors (NCT05497453).

About the OMEGA platform

The OMEGA platform leverages the Company's deep understanding of gene regulation, genomic architecture and epigenetic mechanisms to design programmable epigenomic mRNA medicines that precisely target and modulate gene expression at the pre-transcriptional level. Combining world-class data science capabilities with rational drug design and customized delivery, the OMEGA platform enables control of fundamental epigenetic processes and reprogramming of cellular physiology to address the root cause of disease. Omega's modular and programmable mRNA

medicines, called epigenomic controllers, target specific genomic loci within insulated genomic domains with high specificity to durably tune single or multiple genes to treat and cure diseases through unprecedented precision epigenomic control.

About Omega Therapeutics

Omega Therapeutics is a clinical-stage biotechnology company pioneering the development of a new class of programmable epigenomic mRNA medicines to treat or cure a broad range of diseases. By pre-transcriptionally modulating gene expression, Omega's approach enables precision epigenomic control of nearly all human genes, including historically undruggable and difficult-to-treat targets, without altering native nucleic acid sequences. Founded in 2017 by Flagship Pioneering following breakthrough research by world-renowned experts in the field of epigenetics, Omega is led by a seasoned and accomplished leadership team with a track record of innovation and operational excellence. The Company is committed to revolutionizing genomic medicine and has a pipeline of therapeutic candidates derived from its OMEGA platform spanning oncology, regenerative medicine, and multigenic diseases including inflammatory and cardiometabolic conditions.

For more information, visit omegatherapeutics.com, or follow us on X and LinkedIn.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements regarding the versatile capabilities and power of the OMEGA platform, the potential of Omega's approach to precision epigenomic control and the ability of OTX-2002 to controllably regulate the historically undruggable MYC gene in multiple models of HCC, the wide spectrum of possibilities to apply precision epigenomic control as a novel therapeutic modality to meaningfully address key drivers of many diseases, and the potential of the Company's pipeline of therapeutic candidates. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: the novel technology on which our product candidates are based makes it difficult to predict the time and cost of preclinical and clinical development and subsequently obtaining regulatory approval, if at all; the substantial development and regulatory risks associated with epigenomic controllers due to the novel and unprecedented nature of this new category of medicines; our limited operating history; the incurrence of significant losses and the fact that we expect to continue to incur significant additional losses for the foreseeable future; our need for substantial additional financing; volatility in capital markets and general economic conditions; our investments in research and development efforts that further enhance the OMEGA platform, and their impact on our results; uncertainty regarding preclinical development, especially for a new class of medicines such as epigenomic controllers; potential delays in and unforeseen costs arising from our clinical trials; the fact that our product candidates may be associated with serious adverse events, undesirable side effects or have other properties that could halt their regulatory development, prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences; difficulties manufacturing the novel technology on which our epigenomic controller candidates are based; our ability to adapt to rapid and significant technological change; our reliance on third parties for the manufacture of materials; our ability to successfully acquire and establish our own manufacturing facilities and infrastructure; our reliance on a limited number of suppliers for lipid excipients used in our product candidates; our ability to advance our product candidates to clinical development; and our ability to obtain, maintain, enforce and adequately protect our intellectual property rights. These and other important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the quarter ended June 30, 2024, and our other filings with the SEC, could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. Any such forward-looking statements represent management's estimates as of the date of this press release. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change.

Contact Investor contact: Eva Stroynowski 617.949.4370 estroynowski@omegatx.com Media contact: Jason Braco 646.751.4361 jbraco@lifescicomms.com